

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Soff *et al.*

Application No.: 08/991,761

Group Art Unit: 1642

Filed: December 16, 1997

Examiner: Minh-Tam B. Davis

For: METHODS AND COMPOSITIONS
FOR GENERATING ANGIOSTATIN

Supervisory Examiner: Anthony C. Caputa

Attorney Docket No.: 10561-004

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**SECOND SUPPLEMENTAL DECLARATION OF
GERALD A. SOFF, M.D., UNDER 37 CFR § 1.132**

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

GERALD A. SOFF M.D. declares and states that:

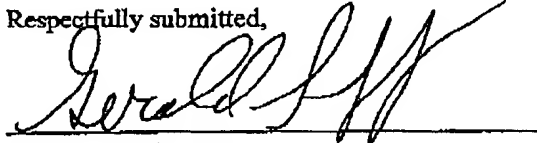
1. I am a citizen of the United States, residing at 303 Apple Tree Lane, Wilmette, IL 60091 and a coinventor of present U.S. Patent Application No. 08/991,761, filed 12/16/97, in the name of Soff *et al.* and entitled "Methods and Composition For Generating Angiostatin," the same coinventor who has previously submitted declarations in connection with the above-identified application.
2. I am submitting this Declaration in response to a request made by Examiner Davis and supervisory Examiner Caputa during a telephone interview that occurred on October 3, 2002, to clarify the activity of plasminogen activator when used in human patients.
3. The data submitted to the U.S.P.T.O. demonstrates that the administration of plasminogen activator without sulfhydryl donor generates angiostatin in human patients.
4. When administered without a sulfhydryl donor, the dose and dosage regimen of plasminogen activator can be adjusted to generate levels of angiostatin that have a clinical benefit in patients with malignant neoplastic disease.

5. I declare further that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date

10/7/02

Respectfully submitted,

A handwritten signature in dark ink, appearing to read "Gerald A. Soff", written over a horizontal line.

Gerald A. Soff, M.D.